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**Electrically guiding migration of human induced pluripotent stem cells.**

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**Funding Grants:** Directing migration of human stem cells with electric fields

**Public Summary:**

The authors developed a new techniques to facilitate stem cell therapy. They used electric fields to guide migration of human induced pluripotent stem cells. This type of cells can be derived from cells from adult body tissues, including skin, and are expected to offer great hope for stem cell therapy. It is difficult to stimulate migration of those cells in the body to repair damage. The authors used small applied electric fields and are able to effectively guide migration of these stem cells.

**Scientific Abstract:**

A major road-block in stem cell therapy is the poor homing and integration of transplanted stem cells with the targeted host tissue. Human induced pluripotent stem (hiPS) cells are considered an excellent alternative to embryonic stem (ES) cells and we tested the feasibility of using small, physiological electric fields (EFs) to guide hiPS cells to their target. Applied EFs stimulated and guided migration of cultured hiPS cells toward the anode, with a stimulation threshold of  $<30$  mV/mm; in three-dimensional (3D) culture hiPS cells remained stationary, whereas in an applied EF they migrated directionally. This is of significance as the therapeutic use of hiPS cells occurs in a 3D environment. EF exposure did not alter expression of the pluripotency markers SSEA-4 and Oct-4 in hiPS cells. We compared EF-directed migration (galvanotaxis) of hiPS cells and hES cells and found that hiPS cells showed greater sensitivity and directedness than those of hES cells in an EF, while hES cells migrated toward cathode. Rho-kinase (ROCK) inhibition, a method to aid expansion and survival of stem cells, significantly increased the motility, but reduced directionality of iPS cells in an EF by 70-80%. Thus, our study has revealed that physiological EF is an effective guidance cue for the migration of hiPS cells in either 2D or 3D environments and that will occur in a ROCK-dependent manner. Our current finding may lead to techniques for applying EFs in vivo to guide migration of transplanted stem cells.

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